Differentiation of multipotent vascular stem cells contributes to vascular diseases.

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Public Summary:
It is generally accepted that the de-differentiation of smooth muscle cells, from the contractile to the proliferative/synthetic phenotype, has an important role during vascular remodelling and diseases. Here we provide evidence that challenges this theory. We identify a new type of stem cell in the blood vessel wall, named multipotent vascular stem cells. Multipotent vascular stem cells can differentiate into neural cells and mesenchymal stem cell-like cells that subsequently differentiate into smooth muscle cells. Lineage tracing demonstrates that neither multipotent vascular stem cells nor proliferative or synthetic smooth muscle cells arise from the de-differentiation of mature smooth muscle cells. In response to vascular injuries, multipotent vascular stem cells, instead of smooth muscle cells, become proliferative, and differentiate into smooth muscle cells and chondrogenic cells, thus contributing to vascular remodelling and neointimal hyperplasia. These findings support a new hypothesis that the differentiation of multipotent vascular stem cells, rather than the de-differentiation of smooth muscle cells, contributes to vascular remodelling and diseases.

Scientific Abstract:
It is generally accepted that the de-differentiation of smooth muscle cells, from the contractile to the proliferative/synthetic phenotype, has an important role during vascular remodelling and diseases. Here we provide evidence that challenges this theory. We identify a new type of stem cell in the blood vessel wall, named multipotent vascular stem cells. Multipotent vascular stem cells express markers, including Sox17, Sox10 and S100beta, are cloneable, have telomerase activity, and can differentiate into neural cells and mesenchymal stem cell-like cells that subsequently differentiate into smooth muscle cells. On the other hand, we perform lineage tracing with smooth muscle myosin heavy chain as a marker and find that multipotent vascular stem cells and proliferative or synthetic smooth muscle cells do not arise from the de-differentiation of mature smooth muscle cells. In response to vascular injuries, multipotent vascular stem cells, instead of smooth muscle cells, become proliferative, and differentiate into smooth muscle cells and chondrogenic cells, thus contributing to vascular remodelling and neointimal hyperplasia. These findings support a new hypothesis that the differentiation of multipotent vascular stem cells, rather than the de-differentiation of smooth muscle cells, contributes to vascular remodelling and diseases.